· At page 99, line 32, please delete "respose " and insert in its stead
   - - response - -.

In the Claims, please enter the following amendments:

1. (amended) A method for predicting a [patient] response of a patient to a treatment of unipolar depression from at least one pre-treatment clinical symptom, comprising:
   a.) performing at least one measurement of said pre-treatment clinical [a] symptom on said patient and measuring said pre-treatment clinical symptom at selected time intervals so as to derive a baseline patient profile;
   b.) defining a set of a plurality of predictor variables which define a set of [the] data of said [the] baseline patient profile, said set of predictor variables comprising predictive symptoms and a set of treatment options;
   c.) deriving a model that represents a [the] relationship between said [patient] response and said [the] set of predictor variables; and
   d.) utilizing the model of step c) to predict the response of said patient to said [the] treatment.

15. (amended) A method of treating depression in a patient comprising the following steps:
   a.) defining a set of predictor variables which define a set of [the] data of a baseline patient profile, said set of predictor variables comprising predictive symptoms and a set of treatment options;
   b.) developing an outcome prediction for said set of treatment options, said outcome prediction based upon [up] an analysis of patient symptoms;
   c.) selecting a first preferred treatment option from said set of treatment options based on said outcome prediction;
   d.) applying said first preferred treatment option to said [the] patient; and
   e.) monitoring said [the] patient by comparing a response of said [the] patient to said treatment option to said outcome prediction to provide an updated outcome prediction for said [the]patient.

16. (amended) The method of claim 15 further including the step of
selecting <u>and applying </u>a second preferred treatment option from said
set of treatment options based on said updated outcome prediction
<u>when said updated outcome prediction and said outcome prediction
differ</u>.

Please add the following claims:

17.   A method for treating a disorder which is diagnosed and
monitored, based upon symptoms experienced by a patient, wherein
patient response to treatment is variable, comprising:

a.) selecting a first treatment regime for a patient who is
diagnosed with said disorder and is exhibiting at least one
observed symptom;

b.) using a recovery modeling system, for modeling expected
recovery patterns for individual patterns of symptoms and
responses to at least one treatment option, to generate an
expected recovery pattern for said patient based upon said
observed symptom and said first treatment regime, said
expected recovery pattern having an expected recovery time
period;

c.) applying said treatment regime to said patient during
said expected recovery time period and monitoring said
patient to develop an actual recovery pattern; and

d.) comparing said actual recovery pattern with said
expected recovery pattern.

18.   The method of claim 17 further comprising reevaluating
said treatment regime at a time interval during said actual
recovery period and if said actual recovery pattern does not
correspond with said expected recovery pattern, discontinuing
said first treatment regime and applying a second treatment

regime.

19.   The method of claim 17 wherein said modeling is non-linear.

20.   The method of claim 17 wherein said modeling is linear second order.

21.   A method for developing a treatment regime for a patient having a disorder which is diagnosed and monitored, based upon at least one observable patient symptom, wherein patient response to treatment is variable, comprising:

> a.)deriving a model of expected recovery patterns for individual patterns of known symptoms and known responses to at least one treatment option;

> b.)selecting a first proposed treatment option for a patient who is diagnosed with said disorder and is exhibiting at least one observed symptom;

> c.)applying said observed symptom and said first proposed treatment option to said model, wherein said model generates a first expected recovery pattern for said patient; and

> d.)reviewing said first expected recovery pattern in order to evaluate the suitability of said first proposed treatment option for said patient.

22. A method for generating an expected recovery pattern for a patient having a disorder which is diagnosed and monitored, based upon patient symptoms, wherein patient response to treatment is variable, and wherein said patient exhibits at least one observed symptom, comprising:

> a.)deriving a model of expected recovery patterns from individual patterns of known symptoms and known responses to at least one treatment option; and

    b.)applying said observed symptom and a proposed
    treatment option to said model wherein said model
    generates an expected recover pattern for said patient.

23. The method of claim 22, further comprising providing a data
    system to integrate data comprising known symptoms,
    treatments and responses thereto, said data provided to said
    model, so that said model can generate generalized expected
    patterns of outcome for a selected treatment when a particular
    pattern of symptoms is exhibited.

24. The method according to claim 22, wherein said model is non-
    linear.

25. The method according to claim 24, wherein said model comprises
    a neural network.

26. The method according to claim 25, wherein said neural
    network has at least   three layers and at least two hidden units,
    and wherein said at least one algorithm is a backpropagation
    learning algorithm.

27. The method according to claim 24, wherein said model is derived
    via quadratic regression.

28. The method according to claim 27, wherein said patient is
    exhibiting a first observed symptom and a second observed
    symptom, and further comprising using an independent variable
    in said quadratic regression, said variable representing an
    interaction between said first observed symptom and said second
    observed symptom.

29.   The method according to claim 28, further comprising
    estimating said interaction by multiplying symptom severities.

30.   The method according to claim 22, further comprising

utilizing said model of expected recovery patterns to rank known symptoms by response influence to indicate the predictive importance of a particular known symptom.

31.   The method according to claim 30, wherein said model is a multilayer neural network utilizing a back propagation learning algorithm having three layers and two hidden units, and an output; and said influence of a known symptom determined by summing a first product and a second product,

> said first product being a first weight from said known symptom to a first hidden unit multiplied by a second weight from said first hidden unit to said output, and

> said second product being a third weight from said known symptom to a second hidden unit multiplied by a fourth weight from said second hidden unit to said output.

32.   The method according to claim 22, wherein said disorder is unipolar depression, and predictive symptoms comprise a plurality of Mood, Energy, and Work.

33.   The method according to claim 22, wherein said disorder is unipolar depression, and predictive symptoms comprise a plurality of Mood, Cognitions, and Work..

34.   The method according to claim 22, further comprising: before deriving said model, providing a set of known baseline patient profiles and treatment outcomes, which known profiles and outcomes are used to derive said model.

35.   The method according to claim 22, wherein for a first known response, a first known recovery pattern is interpolated from data about said first known response.

36.   A method of treating a disorder which is diagnosable and treated based upon a patient's symptom and for which a patient

could have a variable response to treatment, comprising:

    a.)   developing an outcome prediction for a set of treatment options and an integrated expected recovery pattern for each treatment option in said set of treatment options, said outcome prediction and said integrated expected recovery pattern for each said treatment option based on an analysis of known patient symptoms and recovery patterns;

    b.)selecting for said patient a first preferred treatment option from said set of treatment options;

    c.)generating a first expected recovery pattern associated with said first preferred treatment option, said first expected recovery pattern having a first expected recovery time period;

    d.)applying said first preferred treatment option to said patient;

    e.)monitoring said patient during said first expected recovery time period to develop a patient treatment response;

    f.)comparing said patient treatment response and said first expected recovery pattern; and

    g.)selecting a second preferred treatment option from said set of treatment options when said patient treatment response varies significantly from said first expected recovery pattern thereby defining a treatment intervention for said patient.

37.   The method according to claim 36, wherein the monitoring of step e.) comprises developing an individual patient recovery profile, and the comparing of step f.) and the selecting of step g.)

comprise:

a.)developing a difference between said individual patient recovery profile;

b.)determining whether said difference is within an acceptable range, indicating a normal patient recovery;

c.)determining whether said difference is outside said acceptable range, indicating an unacceptable patient recovery pattern; and

d.)selecting a second preferred treatment option from said set of treatment options when said difference is outside said acceptable range.

38. The method according to claim 36, wherein the monitoring comprises assessing said observed symptoms of said patient at various time intervals during said first expected recovery time period.

39. A method for facilitating selection of a treatment regime for a disorder which is diagnosed and monitored, based upon symptoms experienced by a patient, wherein the patient response to said treatment is variable, comprising:

a.)providing a modeling system;

b.)generating at least one expected recovery pattern for a patient exhibiting a particular set of symptoms, each said expected recovery pattern associated with a particular treatment option;

c.)analyzing said expected recovery patterns to determine the suitability of each associated particular treatment option for said patient; and

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d.)developing a treatment regime from said analysis.

40. The method of claim 39, wherein said modeling system comprises:

a.)inputting into a model a set of data comprising a plurality of individual patterns of symptoms and responses to at least one treatment option; and

b.)analyzing said set of data with said model to generate said expected recovery patterns.

41. The method of claim 39 wherein said modeling system comprises a non-linear second order differential equation model representing a recovery pattern by parameters indicative of a treatment intervention effect, a recovery latency, and a symptom interaction effect.

42. The method according to claim 36, wherein said treatment intervention is represented by an immediate effect and a delayed effect,

said immediate effect represented by a step function, which step function coincides with the onset of treatment;

said delayed effect represented by a sigmoid function of time, with delay and steepness of the onset of the delayed effect.

43. The method according to claim 41, wherein said recovery latency for a particular symptom is based on the time it takes for the intensity of the modeled symptom to decrease halfway from its pretreatment intensity to its intensity after six weeks of treatment.

44. The method according to claim 38, wherein said disorder is unipolar depression, and said symptoms comprise Early Sleep, Middle and Late Sleep, Energy, Work, Mood, Cognition, and

Anxiety.

45. The method according to claim 41, wherein said non-linear second order differential equation model comprises a neural network that is trained to optimize parameter values with said parameter values adjusted through teaching so that the difference between the model output and patient data decreases.

46. The method according to claim 45, wherein said teaching comprises obtaining a set of teaching data, each said set of teaching data comprising known patient pre-treatment symptoms and recovery patterns; inputting each said set of teaching data into said neural network; and making said neural network learn each said set of teaching data.

47. The method according to claim 45, wherein generating said expected recovery pattern comprises:

   obtaining a set of testing data from said patient, said set of testing data comprising test patient pre-treatment symptoms;

   inputting said set of testing data into said neural network and obtaining therefrom an expected recovery pattern for said patient.

48. The method according to claim 46, further comprising updating said teaching data to modify and update said expected recovery patterns to provide a predictive pattern of recovery for individual patterns of symptoms and responses to treatment.

49. A method for monitoring the effectiveness of an assigned treatment for a disorder which is diagnosed and monitored, based upon a plurality of symptoms experienced by a patient, wherein a patient's response to said assigned treatment is variable, said method comprising:

   a.) generating a profile for patient monitoring using the time-

series profile of progress;
b.) assessing at various time intervals; and
c.) timely intervening in said treatment when said treatment is not progressing in accordance with said profile.

50.   A method of selecting a treatment regime to administer to a patient for a disorder which is diagnosable and treatable based upon a patient's symptoms and for which said patient could have a plurality of different patterns of response to said treatment regime, said method comprising:

a.) developing a clinical database containing clinical data from a series of historical patients diagnosed with said disorder, said clinical data comprising pretreatment symptoms, treatments, and responses thereto, of said historical patients;
b.) developing a symptom profiler from said clinical data, said symptom profiler generating a known recovery pattern over time, said known recovery pattern based upon measurements of selected symptoms, said known recovery pattern associated with a selected treatment regime;
c.) developing a predictive database from said symptom profiler, said predictive database containing predicted outcomes in response to said treatment regimes;
d.) performing at least one measurement of a symptom on said patient diagnosed with said disorder so as to derive a baseline patient profile; and
e.) applying said baseline patient profile to said symptom profiler in order to generate said treatment regime and a predicted outcome for said patient.

51.   The method of claim 50, further comprising providing a model system to integrate said clinical data.

52.   The method of claim 51 further comprising providing a processing unit that weights said clinical data, each unit of clinical data weighted to represent the strength of the effect of said unit of clinical data.

53.   The method of claim 52, wherein each unit of clinical data has
an activation value which is passed through a function to produce
an output.

54.   An automated system for generating an expected recovery
pattern for a patient having a disorder which disorder is
diagnosed and monitored, based upon patient symptoms, wherein
patient response to treatment is variable, and wherein said
patient is exhibiting at least one observed symptom, said
automated system comprising a modeling system for modeling
individual expected recovery patterns for individual patterns of
known symptoms and known responses to at least one treatment
option, to which said observed symptom and a proposed
treatment option are applied, said modeling system generating an
expected recovery pattern for said patient, said modeling system
having a neural network architecture comprising:

a.) an input;
b.) a network node for each symptom in a set of symptoms for
said disorder;
c.) a delay node transfer function box to represent a latency of
a response to said each treatment;
d.) an immediate response treatment pathway connected to
said input and said delay node transfer function box;
e.) a latent response treatment pathway connected to said
input and said delay node transfer box;
f.) a first set of uni-directional connections, having a first
subset and a second subset, said connections representing an
associated effect for each treatment in a set of treatment
options; said first subset from said immediate response
treatment pathway to said nodes and said second subset from
said delay node transfer function box to said nodes; and
g.) a second set of bi-directional connections between said
nodes representing symptom interactions.

55.   The system of claim 54, wherein each of said network nodes

represents an intensity of each of said symptoms.

56. The system of claim 54 wherein said uni-directional connections are weighted to represent an intensity of each of said effects.

57. The system of claim 54 wherein said bi-directional connections are weighted in each direction to represent intensities of said symptom interactions.

58. The system of claim 54 wherein said delay node transfer function box comprises a delay node that is a sigmoid function having parameters that comprises length of delay and steepness of onset of said delayed effect.

59. The system of claim 54 wherein said immediate response treatment pathway is represented by a step function fixed to coincide with the onset of treatment.

Comments

Amendments to the specification have been made to correct spelling errors and to remove spurious computer added characters such as "}" "\", "{", ">" and "$".

The form of the citations in the Specification to references has been changed to conform to US Patent and Trademark Office practices. The basis for the expanded citations may be found in Table 4.2 in the drawings papge 20 of 21 and in the Bibliography of Luciano, US Provisional Application S.N. 60/041,287 which is incorporated by reference in the above identified application.

The amendment to claim 16 finds basis at page 11, lines 29-31 of the above identified application.

Added claim 17 finds basis at page 11 and throughout the Specification and in the figures pages 1 to 11 of the above identified application.

Added claim 18 finds basis at page 11, lines 29-31 and in figure 1 b.

Added claim 19 finds basis at pages 17-18, 66, 77-79 and in the figures of the Specification.

Added claim 20 finds basis at pages 13, 17, 22.

Added claim 21 finds basis at page 11, figures 1 to 11, and throughout the Specification.

Added claim 22 finds basis at page 11, figures 1 to 11, and throughout the Specification.

Added claim 23 finds basis at figs. 1 a, 1 b, 2 and at pages 7-9, 11.

Added claim 24 finds basis at pages 17-18, 66, 77-79.

Added claim 25 finds basis at page 66.

Added claim 26 finds basis at page 77.

Added claim 27 finds basis at page 77, 79

Added claim 28 finds basis at page 88.

Added claim 29 finds basis at pages 96-97.

Added claim 30 finds basis at pages 85-86.

Added claim 31 finds basis at page 86.

Added claim 32 finds basis at page 47-62.

Added claim 33 finds basis at page 47-62.

Added claim 34 finds basis at page 11 and Fig. 2.

Added claim 35 finds basis at Fig. 2.

Added claim 36 finds basis at page 11, Figs. 1 b and 2, and throughout the Specification.

Added claim 37 finds basis at pages 7-9, 11-12, 45, 65-66, Fig. 3-9.

Added claim 38 finds basis at pages 7-9, 11-12.

Added claim 39 finds basis at Figs. 1 b and 2 and throughout the Specification.

Added claim 40 finds basis at Fig. 1a, 2, and 3-4.

Added claim 41 finds basis at Fig. 3-4., pages 41-44, 85-92

Added claim 42 finds basis at Fig. 3-4 and pages 17-19

Added claim 43 finds basis at page 20.

Added claim 44 finds basis at pages 47-62.

Added claim 45 finds basis at pages 26-38, figs. 1 a, 1 b, 3-2.

Added claim 46 finds basis at pages 26-38, figs. 1 a, 1 b, 3-2.

Added claim 47 finds basis at fig.2.

Added claim 48 finds basis at page 11, lines 14-16.

Added claim 49 finds basis at page 11 and throughout the Specification.

Added claim 50 finds basis at pages 7-9, 11-12, figs. 1 a, 1 b, 2, and throughtout the Specification.

Added claim 51 finds basis at pages 7-9, 11-12.

Added claim 52 finds basis at fig. 1 c and at pages 7-9, 11-12.

Added claim 53 finds basis at fig. 1 c and at pages 7-9, 11-12.

Added claim 54 finds basis at fig. 3-3, 3-4 and at pages 7-9, 11-12, 17-22 and throughout the Specification.
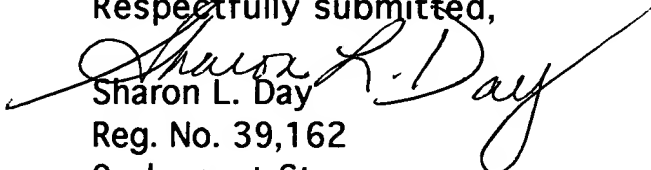
Added claims 55-59 finds basis at fig. 3-3, 3-4 and at pages 7-9, 11-12, 23-24, 26-45.

The above amnedments are believed to put the application in condition for allowance. No new matter is believed to have been added.

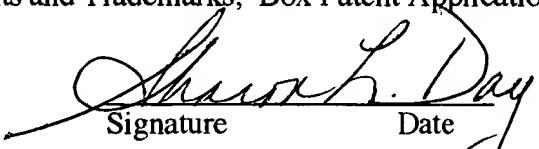A Fee of $716 is being submitted herewith to pay for the additional claims.

If the Examiner has any questions or comments, please contact Sharon L. Day, Agent for the Application at (781) 784- 9602 or (617) 441-5177. (E-mail: sharon_day@sharon.k12.ma.us).

Respectfully submitted,

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CERTIFICATION OF FiRST CLASS MAILING

I hereby certify that this Preamendment and the documents referred to as enclosed herein are being deposited with the United States Postal Service on the date 7/24/98 , in an envelope as "First Class Mail" addressed to the Commissioner of Patents and Trademarks, Box Patent Applications, Washington, DC 20231.

Signature   Date

7/24/98

Fee calculation
59-20 = 39 X 11 = $429
7 X 41 =   287
TOTAL $716